DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 02N–0418]

DMB Display Date 1-22-03
Publication Date 1-23-03
Certifier R. LEDESMA

Agency Information Collection Activities; Submission for OMB Review; Comment Request; Adverse Experience Reporting for Licensed Biological Products; and General Records

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing that the proposed collection of information listed below has been submitted to the Office of Management and Budget (OMB) for review and clearance under the Paperwork Reduction Act of 1995.

DATES: Submit written comments on the collection of information by [*insert date 30 days after date of publication in the* **Federal Register**].

ADDRESSES: Submit written comments on the collection of information to the Office of Information and Regulatory Affairs, OMB, New Executive Office Bldg., 725 17th St. NW., rm. 10235, Washington, DC 20503, Attn: Stuart Shapiro, Desk Officer for FDA.

FOR FURTHER INFORMATION CONTACT: JonnaLynn P. Capezzuto, Office of Information Resources Management (HFA–250), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–4659.

SUPPLEMENTARY INFORMATION: In compliance with 44 U.S.C. 3507, FDA has submitted the following proposed collection of information to OMB for review and clearance.

Adverse Experience Reporting for Licensed Biological Products (OMB Control Number 0910–0308)—Extension

Under the Public Health Service Act (42 U.S.C. 262), FDA is required to ensure the marketing of only those biological products that are safe and effective. FDA must, therefore, be informed of all adverse experiences occasioned by the use of licensed biological products. FDA issued the adverse experience reporting (AER) requirements in part 600 (21 CFR part 600) to enable FDA to take actions necessary for the protection of the public health in response to reports of adverse experiences related to licensed biological products. The primary purpose of FDA's AER system is to flag potentially serious safety problems with licensed biological products, focusing especially on newly licensed products. Although premarket testing discloses a general safety profile of a new drug's comparatively common adverse effects, the larger and more diverse patient populations exposed to the licensed biological product provides the opportunity to collect information on rare, latent, and long-term effects. Reports are obtained from a variety of sources, including patients, physicians, foreign regulatory agencies, and clinical investigators. Information derived from the AER system contributes directly to increased public health protection because such information enables FDA to recommend important changes to the product's labeling (such as adding a new warning), to initiate removal of a biological product from the market when necessary, and to assure the manufacturer has taken adequate corrective action if necessary.

The regulation in § 600.80(c)(1) requires the licensed manufacturer to report each adverse experience that is both serious and unexpected, regardless of source, as soon as possible, but in any case, within 15 working days of initial

receipt of the information. Section 600.80(e) requires licensed manufacturers to submit a 15-day alert report obtained from a postmarketing clinical study only if there is a reasonable possibility that the product caused the adverse experience. Section 600.80(c)(2) requires the licensed manufacturer to report each adverse experience not reported under paragraph (c)(1) at quarterly intervals, for 3 years from the date of issuance of the product license, and then at annual intervals. The majority of the periodic reports will be submitted annually since a large percentage of the current licensed biological products have been licensed longer than 3 years. Section 600.80(i) requires the licensed manufacturer to maintain for a period of 10 years records of all adverse experiences known to the licensed manufacturer, including raw data and any correspondence relating to the adverse experiences. Section 600.81 requires the licensed manufacturer to submit information about the quantity of the product distributed under the product license, including the quantity distributed to distributors at an interval of every 6 months. The semiannual distribution report informs FDA of the quantity, the lot number, and the dosage of different products.

Section 600.90 requires a licensed manufacturer to submit a waiver request with supporting documentation when asking for waiving the requirement that applies to them under §§ 600.80 and 600.81. Manufacturers of biological products for human use must keep records of each step in the manufacture and distribution of products including recalls of the product. The recordkeeping requirements serve preventative and remedial purposes. These requirements establish accountability and traceability in the manufacture and distribution of products, and enable FDA to perform meaningful inspections.

Section 600.12 requires that all records of each step in the manufacture and distribution of a product be made and retained for no less than 5 years after the records of manufacture have been completed or 6 months after the latest expiration date for the individual product, whichever represents a later date. In addition, records of sterilization of equipment and supplies, animal necropsy records, and records in cases of divided manufacturing of a product are required to be maintained. Section 600.12(b)(2) requires complete records to be maintained pertaining to the recall from distribution of any product. Respondents to this collection of information are manufacturers of biological products. Under table 1 of this document, the number of respondents is based on the estimated number of manufacturers that submitted the required information to FDA in the years 2000 and 2001. Based on information obtained from the Center for Biologics Evaluation and Research's (CBER's) database system, there were approximately 95 licensed manufacturers. This number excludes those manufacturers who produce blood and blood components and in vitro diagnostic licensed products because they are specifically exempt from the regulations. However, not all manufacturers may have any submissions in a given year and some may have multiple submissions. The total annual responses are based on the estimated number of submissions received annually by FDA. There were an estimated 13,938 15-day alert reports, 10,102 periodic reports, and 339 distribution reports submitted to FDA. The number of 15-day alert reports for postmarketing studies as stated in § 600.80(e) was minimal and is included in the total number of 15-day alert reports. FDA received an average of 12 waiver requests under § 600.90, of which 11 were approved for exemption of the AER requirements. The hours per response are based on FDA's experience. The burden hours required to complete the MedWatch Form

for § 600.80(c)(1), (e), and (f) are reported under OMB control number 0910–0291.

In the **Federal Register** of October 4, 2002 (67 FR 62249), FDA published a 60-day notice requesting public comment on the information collection provisions. No comments were received.

TABLE 1.—ESTIMATED ANNUAL REPORTING BURDEN[1]

21 CFR Section	No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
600.80(c)(1) and (e)	95	146.72	13,938	1	13,938
600.80(c)(2)	95	106.34	10,102	28	282,856
600.81	95	3.57	339	1	339
600.90	12	1	12	1	12
Total					297,145

[1] There are no capital costs or operating and maintenance costs associated with this collection of information.

Under table 2 of this document, the number of respondents is based on the number of manufacturers subject to those regulations. Based on information obtained from CBER's database system, there were approximately 329 licensed manufacturers of biological products. However, the number of recordkeepers listed for § 600.12(a) through (e), excluding paragraph (b)(2), is estimated to be 111. This number excludes manufacturers of blood and blood components because their burden hours for recordkeeping have been reported under § 606.160 in OMB control number 0910–0116. The total annual records is based on the annual average of lots released (6,747), number of recalls made (1,646) and total number of AER reports received (24,040) in the years 2000 and 2001. The hours per record are based on FDA's experience. FDA estimates the burden of this recordkeeping as follows:

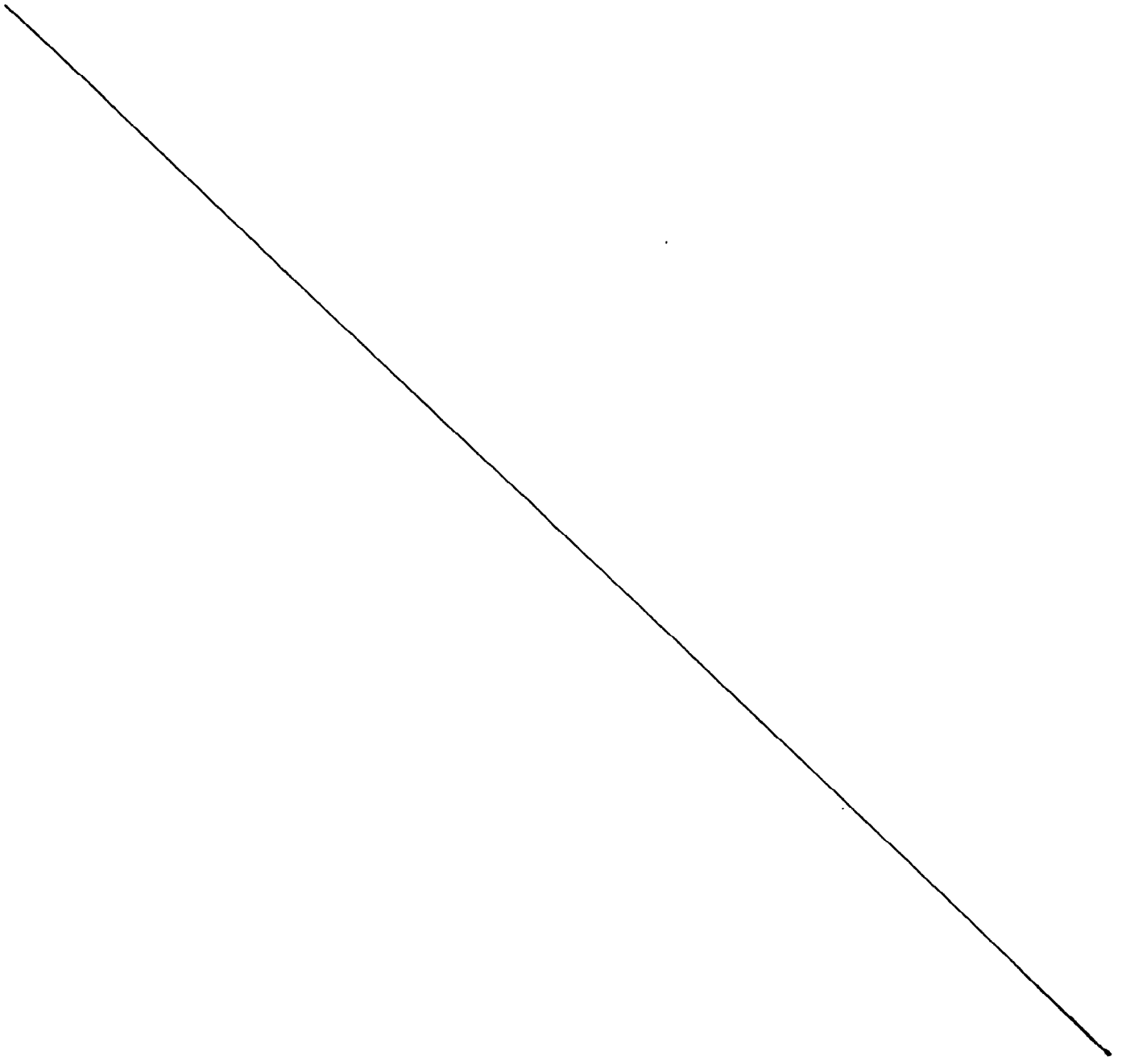
TABLE 2.—ESTIMATED ANNUAL RECORDKEEPING BURDEN[1]

21 CFR Section	No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
600.12	111	60.78	6,747	32	215,904
600.12(b)(2)	329	5.00	1,646	24	39,504
600.80(i)	95	253.05	24,040	1	24,040

TABLE 2.—ESTIMATED ANNUAL RECORDKEEPING BURDEN[1]—Continued

21 CFR Section	No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
Total					279,448

[1] There are no capital costs or operating and maintenance costs associated with this collection of information.



Dated: 1-14-03

January 14, 2003.

Margaret M. Dotzel

Margaret M. Dotzel,
Assistant Commissioner for Policy.

[FR Doc. 03–????? Filed ??–??–03; 8:45 am]

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